

CANCER OF THE CERVIX UTERI

A REVIEW OF 169 NECROPSIED CASES *

RAUL A. MARCIAL-ROJAS, M.D.,† and JOE VINCENT MEIGS, M.D.

*From the Department of Pathology and Gynecology of the Pondville Cancer Hospital
(Massachusetts Department of Public Health), Walpole, Mass.*

It has been demonstrated¹ that radical hysterectomy with bilateral pelvic lymph node dissection can be performed with a very low mortality, small morbidity, and satisfactory results in patients with stage I and stage II carcinoma of the cervix. Recently, attempts have been undertaken to achieve surgical results better than those derived from radiation therapy in stages III and IV. It has been established that radical pelvic exenteration can be accomplished with a mortality of 25 per cent or less and that the resultant physiologic readjustment permits a fairly comfortable and active life.^{2,3} Radical removal of all pelvic viscera for advanced cervical cancer apparently should be limited to patients in whom a chance for cure by any other form of therapy is less than 5 per cent.

For a better understanding of the pathologic features and the actual extent of the disease, we believed that a complete review of the necropsied cases of carcinoma of the cervix which had been treated by radiation would be of great value. From this we hoped to make a better evaluation of the possibilities of ultra-radical surgery. The findings at necropsy should also give us a picture of the life history of cancer of the cervix and perhaps an idea of the value of, and the complications from, radiation therapy.

This report represents the study of 169 cases of carcinoma of the cervix treated by radiation and necropsied at the Pondville Cancer Hospital from 1931 to 1951.

Types and Histologic Grading

From our study it is evident that the significance of histologic grading of neoplasms is far from settled, and is of less importance than the clinical extent of the disease. In determining the histologic grading, a modification of Broders' classification proposed by Warren⁴ was used.

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† Now at Department of Pathology, University of Puerto Rico School of Medicine and the I. Gonzales Martinez Oncologic Hospital, San Juan, P.R.

It divides the epidermoid carcinomas into three groups: grade I, low malignancy; grade II, medium malignancy; and grade III, high malignancy. The histologic criteria are based upon the degree of differentiation of tumor cells, relation of tumor to stroma, and frequency of mitotic figures; the last being considered the most important single

TABLE I
Histopathologic Grading of all Epidermoid Tumors

Grade I		Grade II		Grade III		Total	
No.	%	No.	%	No.	%	No.	%
17	11.5	68	46.2	62	42.1	147	100

TABLE II
Type of Tumor

Epidermoid		Adenocarcinoma		Adeno-acanthoma		Total	
No.	%	No.	%	No.	%	No.	%
147	87.0	13	7.7	9	5.3	169	100

criterion. The average number of mitotic figures per high-power field was established for the purpose largely of eliminating the personal equation. It was considered that an average of less than two mitotic figures per high-power field constituted grade I; from two to four, grade II; and more than four, grade III. The adeno-acanthomas and adenocarcinomas were considered in a separate classification.

In all of the necropsied cases, except two in which no tumor was found, the histologic grading was checked from necropsy material. For the two cases, we used the biopsy slide.

A slightly greater incidence of distant metastases was noted in grade III carcinomas and in the adeno-acanthomas, but no significant difference was noted as to pelvic extension among the grades and types.

Frequently, at necropsy, the pelvic extension of the process could not be determined accurately because of marked fibrosis due to radiation. This change may be difficult to differentiate grossly from neoplastic involvement.

Incidence and Distribution of Distant Metastases

It is well known that carcinoma of the cervix exhibits a low incidence of distant metastases and more often spreads locally into the parametrium, pelvic organs, and pelvic lymph nodes. Lack of spread may be explained partly by the frequent occurrence of early ureteral obstruction with resultant uremia and death and therefore lack of time

for further involvement. In our series, 22.4 per cent of the 169 necropsied cases showed evidence of distant metastases. This figure is slightly lower than those of other reports. The great majority of patients dying of cervical cancer do not have metastases outside the pelvis. In every instance in which there was metastasis to the nodes at the bifurcation of the aorta, distant metastases were found also.

TABLE III

Incidence and Anatomical Distribution of Distant Metastases in Cases of Carcinoma of the Cervix Uteri in Which the Periaortic Lymph Nodes Were Involved

Liver	41 (85.4%)
Lungs	31 (64.5%)
Peritoneum	24 (50.0%)
Bone	14 (29.3%)
Miscellaneous	33 (68.7%)

(22.4% of all cases in the necropsied series exhibited distant metastases.)

TABLE IV

Anatomical Distribution of the 33 Miscellaneous Distant Metastases

Kidney	7
Adrenal gland	7
Intestine	6
Spleen	5
Heart	3
Brain	2
Pancreas	2
Skin	1

TABLE V

Anatomical Distribution of Osseous Metastases

Lumbar vertebrae	14
Dorsal vertebrae	4
Humerus	2
Ribs	1
Skull	1
Femur	1

(8.1% of all cases showed bony metastases; more than one bone was involved in some patients.)

TABLE VI

Incidence of Ureteral Obstruction

Left	18 (15.0%)
Right	16 (13.3%)
Bilateral	86 (71.6%)
Total	120

(71% of the 169 cases showed either bilateral or unilateral ureteral obstruction.)

Distant metastases were not encountered in this series in the absence of periaortic nodal involvement. This observation seems to suggest that the lymphatic system is the usual route through which cervical cancer spreads to distant regions, and the rarity of blood vessel invasion in microscopic sections is supporting evidence. In cases with distant metastases, the lungs were involved in 64.5 per cent and the bones in 29.3 per cent.

Incidence of Ureteral Obstruction

The ureteral and renal complications of carcinoma of the cervix have been recognized since the middle of the last century. In 1858, Wagner⁵ reported that one third of all his cases showed ureteral involvement on examination at necropsy. Williams,⁶ in 1895, reported

an incidence of hydro-ureter and hydronephrosis of 85.9 per cent in 78 necropsies. In the 150 post-mortem examinations of Faerber,⁷ obstructive renal changes were encountered in 72 per cent. Behney,⁸ in 166 cases, reported the incidence of ureteral obstruction as 65 per cent, and the occlusion was sufficient to cause uremia and death in 21 per cent of patients. Warren⁹ ascribed the great majority of deaths in cervical cancer to renal insufficiency of obstructive nature.

Graves, Kickham, and Nathanson,¹⁰ in a very comprehensive analysis of 600 cases of carcinoma of the cervix at the Pondville Cancer Hospital from 1927 to 1935, with 87 necropsies, some of which are included also in the present communication, found ureteral obstruction in over 70 per cent. In this present series 71 per cent of the 169 necropsied patients showed either bilateral or unilateral ureteral obstruction. The obstruction was severe enough to cause uremia and death in 46.1 per cent.

Causes of Death

Our analysis showed that uremia was by far the most frequent cause of death. The second most frequent cause of death was peritonitis.

TABLE VII

Causes of Death in Carcinoma of the Cervix

Uremia	78 (46.1%)
Peritonitis	38 (22.4%)
Pneumonia	11 (6.5%)
Hemorrhage	5 (2.8%)
Intestinal obstruction	3 (1.7%)
Miscellaneous*	35 (20.7%)
Total	169

* In 80% of the miscellaneous group of 35 it was believed that death was due to cachexia and/or carcinomatosis.

TABLE VIII

Incidence of Fistula Formation According to Anatomical Location

Vesico-vaginal	52 (58.4%)
Recto-vaginal	34 (38.2%)
Miscellaneous	3 (3.3%)
Total	89 (100.0%)

Necropsies showed that 22.4 per cent of the cases had peritonitis resulting from post-radiation necrosis and perforation. One of the two cases in which no tumor was found at necropsy had severe radiation fibrosis with necrosis of the bowel and perforation and peritonitis.

In 35 cases, or 20.7 per cent, the immediate cause of death could not be determined accurately; in 80 per cent of these 35 cases death was attributed to cachexia and/or carcinomatosis. Pneumonia accounted for 6.5 per cent of all deaths. Hemorrhage was responsible for only 2.8 per cent, and in all cases was due to tumor invasion and necrosis of the iliac veins. The arteries appeared to be extremely resistant to neoplastic involvement.

Incidence of Fistulas

All cases in this series were treated with radium, so it is not possible to compare the incidence of fistulas with that in a group of untreated cases. Warren⁴ found no significant difference in such groups, namely, 43 per cent of those who had radium treatment and 46 per cent of those with no treatment. At necropsy 67 of our 169 cases showed one fistula, or an incidence of 40 per cent, and 22 of them exhibited two fistulas. The total number with fistulas was 89, or 52 per cent. In many of the cases the tissues surrounding the fistula showed changes which strongly suggested radiation change as the primary cause of the lesion.

SUMMARY AND CONCLUSIONS

In cervical cancer the disease is limited to the pelvis in the majority of the cases, so that theoretically a complete removal of pelvic viscera should be curative.

When a pelvic exenteration is contemplated, a complete study of the patient should be carried out. Roentgenograms of the chest and a radiologic bone survey should be made, and tests of renal function should be performed. Only by a complete examination can unnecessary surgery be avoided.

Accepting the fact demonstrated by this study that metastasis to the lymph nodes at the bifurcation of the aorta is invariably accompanied by distant spread, we recommend that before proceeding with exenteration these nodes should be subjected to pathologic examination. Frozen sections are adequate for this purpose in the hands of a competent surgical pathologist.

Ureteral obstruction was found in 71.0 per cent of this group of necropsied patients. Often the ureteral obstruction was bilateral.

Fistulas are frequent, due either to the progress of the disease or to severe radiation change.

The most frequent causes of death are uremia and peritonitis.

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